REMARKS

Favorable reconsideration of this application, in light of the present amendments and following discussion, is respectfully requested.

Claims 1-5 are pending; Claim 1 is amended; and Claims 4 and 5 are newly added. It is respectfully submitted that no new matter is added by this amendment.

In the outstanding Office Action, Claims 1 and 2 were rejected under 35 U.S.C. § 103(a) as unpatentable over Castle (U.S. Pat. No. 5,429,594) in view of "Photoreduction of Heme Proteins: Spectroscopic Studies and Cross-Section Measurements" (hereafter Gu). Claim 3 was indicated as allowable.

Applicants acknowledge with appreciation the indication that Claim 3 contains allowable subject matter. Because the amendment to Claim 1, from which Claim 3 depends, addresses a minor informality, Claim 3 remains in dependent form.

With regard to the rejection of Claims 1 and 2 under 35 U.S.C. § 103(a) as unpatentable over Castle in view of Gu, that rejection is respectfully traversed.

The present invention, as recited in Claims 1-5, relates to a method for regenerating the oxygen binding ability of hemoglobin, which has been lost through oxidation, in a hemoglobin-vesicle suspension serving as an oxygen infusion (oxygen carrier), thereby maintaining oxygen transporting ability.[1] Due to the difficulties with injecting human blood into a blood vessel, there is presently a great demand for a blood substitute that is available anytime and that replaces all blood types. Electrolyte transfusions and colloidal transfusions have hitherto been widely used as blood substitutes. However, these substitutes are unable to function as erythrocytes for transporting oxygen. Thus, a need exists to develop a substance (oxygen transfusion) to substitute for the oxygen transporting function.[2]

[1] Specification, page 1, lines 15-20.

[2] Id. at page 2, lines 17-27.

To overcome the difficulties described above, the present inventors extensively conducted systematic studies on oxygen infusion with a view toward developing a method of regenerating the oxygen binding abilities of the hemoglobin-vesicles, in the case where methemoglobin is produced.[3]

To this end, independent Claim 1 recites a method of regenerating a lowered oxygen binding ability of a hemoglobin-vesicle suspension to be used as an oxygen infusion includes using, as a hemoglobin-vesicle, a phospholipid vesicle which contains the aqueous hemoglobin solution therein and an electron donor in an inner aqueous phase thereof ... thereby reducing methemoglobin into hemoglobin to regenerate the oxygen binding ability.

Thus, to regenerate methemoglobin into reduced-type hemoglobin by light irradiation, not only hemoglobin solution, but also electron donors are added to the hemoglobin vesicles. Since electron donors are present in the hemoglobin solution, electron migration occurs when the solution is irradiated by light, and reduces the methemoglobin into hemoglobin. Therefore, it is possible to regenerate the oxygen binding ability of hemoglobin.

By virtue of providing electron donors in an inner water phase of the vesicle, as recited in Claim 1, the concentration of electron donors in the inner water phase increases, thereby accelerating a photoreduction reaction of methemoglobin.[4] The advantageous results of the method recited in Claim 1 are evident from comparing Example 2 using a hemoglobin vesicle of the present invention and Comparative Example 1[5] using a methemoglobin solution having an electron donor added therein. In Comparative Example 1 no electron donor is present in the inner water phase.

---

[3] Id. at page 8, lines 11-15.

[4] See, e.g., specification at page 16, lines 8-13.

[5] Id. at page 19.

Castle relates to an extra corporeal blood access, sensing, and radiation methods. However, the techniques described in Castle correspond to the content shown in Comparative Example 1 of the present specification. As previously explained, Comparative Example 1 does not include an electron donor in an inner aqueous phase of the hemoglobin-vesicle, as recited in Claim 1. Additionally, as admitted in the Office Action at page 3, Castle does not disclose or suggest that the irradiation oxidizes hemoglobin into methemoglobin by irradiating hemoglobin.

The outstanding Office Action attempts to remedy the admitted deficiency of Castle by relying on Gu. However, in Gu, UV radiation is used to change *hemoglobin into methemoglobin*, which thereby causes a loss in oxygen-bonding ability. By contrast, as recited in Claim 1, light irradiation is performed not to oxidize hemoglobin into methemoglobin *but to reduce methemoglobin into hemoglobin*. Additionally, Gu does not disclose or suggest an electron donor in an inner aqueous phase of the hemoglobin vesicle, as recited in Claim 1.

Accordingly, as neither Castle nor Gu, either alone or in combination, discloses or suggests the electron donor in an inner aqueous phase, as recited in Claim 1, it is respectfully submitted that Claim 1 patentably distinguishes over both Castle and Gu, either alone or in combination. Additionally, because neither Castle nor Gu discloses or suggests irradiating the suspension with the light when hemoglobin contained in the vesicle is oxidized into methemoglobin and loses its oxygen binding ability, thereby reducing the methemoglobin into hemoglobin to regenerate the oxygen binding ability, it is respectfully submitted that Claim 1 further patentably distinguishes over both Castle and Gu.

Moreover, it is respectfully submitted that there is no basis in the teachings of either Castle or Gu to support the applied combination. Certainly, the Office Action fails to cite to any specific teachings within either reference to support the applied combination. It is

therefore respectfully submitted that the combination of Castle and Gu is based upon hindsight reconstruction, and it is therefore respectfully requested that this rejection be withdrawn.

Consequently, in view of the foregoing discussion and present amendments, it is respectfully submitted that this application is in condition for allowance. An early and favorable action is therefore respectfully requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Katherine D. Pauley

Eckhard H. Kuesters
Attorney of Record
Registration No. 28,870
Katherine D. Pauley
Registration No. 50,607

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
EHK:KDP/bu/dmr
I:\ATTY\KDP\21'S\219388US\219388US AM 2-20-04.DOC